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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,990	01/30/2002	Yizhong Gu	PB0176	6593

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Stephen G. Ryan
Amersham Biosciences
800 Centennial Avenue
Piscataway, NJ 08855

EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/060,990	GU ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *7,12-31,34-38 and 40-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-11,32,33,39,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/29/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments filed January 29, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. The addition of new claims 48 and 49 has been acknowledged.

3. Claims 1-6, 8-11, 32, 33, 39, 48, and 49, SEQ ID NO. 1, are examined on the merits.

4. FINAL OFFICE ACTION.

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

7. This rejection is necessitated by Applicants amendments.

8. Specific to claim 1, lines 7, 10, and 17, claim 2, line 2, and claims 48 and 49, line 5, the limitation of "complete complement" has not been found in the instant specification. Therefore, the new limitation is considered to be new matter because "complete complement" is different

from the disclosed limitation of "complement" in the original claims. Claims 4-6, 8-11, 32, 33, and 39 are rejected for being dependent from claim 1.

LACK OF UTILITY UNDER 35 U.S.C. § 101

9. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

10. The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

11. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

12. This rejection is maintained with respect to claims 1-6, 8-11, 32, 33, and 39 as recited in the previous office action mailed September 30, 2003. The instant rejection has been extended to new claims 48 and 49.

13. This rejection is necessitated by Applicants amendments.

RESPONSE TO ARGUMENT

14. Applicant argues that the claimed invention is 79% amino acid identity, and 86% amino acid similarity to the mouse RGL3 which belongs to the RalGEF family of proteins due to said RGL3 having the RasGEFN, RasGEF, and RA functional domains. Further, it is well known in the art that part of the Ras signaling pathways promote invasion metastasis, and RalGEF-dependent transformation led to highly invasive metastasis. The use of an oncogene or tumor suppresser gene in cancer diagnosis, prognosis, and treatment in cancer patients is well known in the art. The above arguments have been fully considered and found to be unpersuasive as discussed below.

15. It is re-iterated that some data are supplied for several sequences, such as for RGL3 in Tables 1 and 2 on pages 125 and 127, no data therein indicate any specificity regarding the elected SEQ ID NO: 1. The claimed nucleic acid is not supported by a specific asserted utility because the other disclosed uses (not specified for any particular sequence) mentioned in the specification are generally applicable to many nucleic acids. Further, Applicants disclose RGL3

cDNA is closely related to sequences known in the art via BLAST query into the GenBank database (page 126, line 28 to page 129, line 10).

16. Applicant's argument further support the instant rejection of the claimed invention which lacks patentable utility due to said invention not being supported by a specific and substantial utility. The arguments above further supports that the function and biochemical property of the claimed invention have been determined indirectly via sequence homology with sequences well known in the art. The instant specification provides no further characterization of the claimed sequence to lead one of ordinary skill in the art to conclude that said sequence has patentable utility as substantially supported by any specific data directed to the function and biochemical property of the claimed invention.

17. Applicant argues that the claimed invention has the RasGEFN, RasGEF, and RA functional domains which have been implicated in Ras signaling pathways promote invasion metastasis, and RalGEF-dependent transformation led to highly invasive metastasis. Not specific to the functional domains cited above, Applicant further argues that an oncogene or tumor suppresser gene has been used in cancer diagnosis, prognosis, and treatment in cancer patients. However, the instant specification discloses the claimed invention as having sequences that are similar to the RasGEFN, RasGEF, and RA functional domains. The instant specification does not provide any specific disclosure which supports that the claimed invention is directly applicable to cancer diagnosis, prognosis, and treatment in cancer patients. No further information is provided regarding the activity or function of either the polynucleotide or encoded protein, which supports that the claimed invention has utility in cancer diagnosis, prognosis, and treatment in cancer patients.

RE-ITERATION OF REJECTION

18. The critical limitation of claims 1-6, 8-11, 32, 33, 39, 48, and 49 is the polynucleotide SEQ ID NO: 1. While some data are supplied for several sequences, such as for RGL3 in Tables 1 and 2 on pages 125 and 127, no data therein indicate any specificity regarding the elected SEQ ID NO: 1. The claimed nucleic acid is not supported by a specific asserted utility because the other disclosed uses (not specified for any particular sequence) mentioned in the specification are generally applicable to many nucleic acids. The specification states that the polynucleotide sequences may be useful as a hybridization probe (page 27) and antisense inhibitor (page 29). The above-mentioned list of desirable utility for the claimed sequence falls short of a readily available utility. These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the polynucleotide being claimed.

19. Further, the claimed polynucleotide is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, the protein produced as a final product resulting from processes involving the nucleic acid does not have asserted or identified specific and substantial utilities. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved, such as the RGL3 encoded by SEQ ID NO: 1, does not define a "real world" context for use. Similarly, the other listed utilities and asserted utilities

as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to many such compounds.

20. Further, Applicants disclose RGL3 cDNA is closely related to sequences known in the art via BLAST query into the GenBank database (page 126, line 28 to page 129, line 10). It is noted that applicant has identified a sequence which is known in the prior art and which has a stated sequence similarity to the claimed sequence. Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science,

290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here.

CLAIMS REJECTION UNDER U.S.C. § 112, FIRST PARAGRAPH

21. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF ENABLEMENT

22. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed sequence. For a sequence putatively assigned a biological function, even if correct, does not appear to be defined as to what use it is to be applied to. The significance of the sequence is undefined, further rendering it indiscernible how someone of skill in the art would use such an entity.

23. This rejection is maintained with respect to claims 1-6, 8-11, 32, 33, and 39 as recited in the previous office action mailed September 30, 2003. The instant rejection has been extended to new claims 48 and 49.

24. This rejection is necessitated by Applicants amendments.

25. The claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.

RESPONSE TO ARGUMENT

26. Applicant is directed to the response to Applicant's argument to overcome the lack of utility rejection above.

LACK OF WRITTEN DESCRIPTION

27. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

28. This rejection is maintained with respect to claims 1-6, 8-11, 32, 33, and 39 as recited in the previous office action mailed September 30, 2003. The instant rejection has been extended to new claims 48 and 49.

29. This rejection is necessitated by Applicants amendments.

RESPONSE TO ARGUMENT

30. Applicant's amendment to the claims to overcome the instant lack of written description has been acknowledged. However, said amendment has not resolved all the lack of written description issues or has introduce new lack of written description issues as discussed below.

31. The specification discloses SEQ ID NO: 1 which corresponds to DNA encoding RGL3. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are directed to encompass gene sequences, sequences that are degenerate variants and sequences encoding a polypeptide at least 90%, 95%, or 99% identical in sequence to the polypeptide of SEQ ID NO. 3. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

> Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

32. With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

33. Therefore, only SEQ ID NO: 1 but not the full breadth of the claims 1-6, 8-11, 32, 33, 39, 48, and 49 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 1, 2, 4-6, 8-11, 48, and 49 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Shao et al. (2000).

34. This rejection is maintained with respect to claims 1, 2, 4-6, 8-11 as recited in the previous office action mailed September 30, 2003. The instant rejection has been extended to new claims 48 and 49.

3. This rejection is necessitated by Applicants amendments.

RESPONSE TO ARGUMENT

35. Applicant's argument via amendment to overcome the instant prior art rejection has been fully considered and found to be unpersuasive because said amendment introduces limitations that have been considered to be new matter as discussed above. Therefore, the new limitations have been withdrawn from consideration in regard to the instant prior rejection.

36. Shao et al. discloses a nucleic acid that encodes RGL3 protein, an effector for Rit and Ras, wherein the nucleotide sequence (AF237669, 2.2 kb) of less than 100 kb in length. The

nucleotide sequence of Shao et al. (position 1-6) is complementary SEQ ID NO. 1 (position 12-17) of the instant application, as in claims 1, 2, 48, and 49.

37. A nucleic probe of the AF237669 sequence is labeled with $^{[32]}P$ and attached to a substrate (page 26915, column 2, Northern Blotting §), as in instant claims 4-6.

The AF237669 sequence has been sub-cloned into expression vector wherein it is linked to a promoter and transformed into a host cell (page 26915, column 1, Two-hybrid Screen § and column 2, Construction of Plasmid Construction §), as in instant claims 8-11.

CONCLUSION

38. NO CLAIM IS ALLOWED.

39. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

40. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

41. This application contains claims 7, 12-31, 34-38, and 40-47 drawn to an invention nonelected with traverse, filed August 11, 2003. A complete reply to the final rejection must

include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

42. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

43. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

44. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

45. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly

4/9/04

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER
4/17/04